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**March 17, 2003**

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**APPLICATION NUMBER: 60/392,514**

**FILING DATE: June 28, 2002**

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PTO/SB/16 (8-00)

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# **PROVISIONAL APPLICATION FOR PATENT COVER SHEET**

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

INVENTOR(S)					
Given Name (first and middle (if any))		Family Name or Surname		Residence (City and either State or Foreign Country)	
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<input checked="" type="checkbox"/> Additional inventors are being named on the <u>1</u> separately numbered sheets attached hereto					
TITLE OF THE INVENTION (280 characters max)					
MANAGEMENT OF DYSPEPSIA AND GASTRIC COMPLIANCE					
Direct all correspondence to: CORRESPONDENCE ADDRESS					
<input type="checkbox"/> Customer Number		<input type="text"/>		<div style="border: 1px solid black; padding: 5px;">Place Customer Number Bar Code Label here</div>	
OR Type Customer Number here					
<input checked="" type="checkbox"/> Firm or Individual Name		ABELMAN, FRAYNE & SCHWAB Attorneys at Law			
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ENCLOSED APPLICATION PARTS (check all that apply)					
<input checked="" type="checkbox"/> Specification Including drawings		Number of Pages		35	<input type="checkbox"/> CD(s), Number
<input type="checkbox"/> Drawing(s)		Number of sheets			<input type="checkbox"/> Other (specify)
<input type="checkbox"/> Application Data Sheet See 37 CFR 1.76					
METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT (check one)					
<input checked="" type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27.					
<input checked="" type="checkbox"/> A check or money order is enclosed to cover the filing fees					
<input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge filing fees or credit any overpayment to Deposit Account Number				01-0035	FILING FEE AMOUNT (\$)
<input type="checkbox"/> Payment by credit card. Form PTO-2038 is attached.					\$80.00
The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.					
<input checked="" type="checkbox"/> No.					
<input type="checkbox"/> Yes, the name of the U.S. Government agency and the Government contract number are:					

Respectfully submitted,

SIGNATURE

TYPED or PRINTED NAME

TELEPHONE

Jay S. Cinamon

(212) 949-9022

Date

June 28, 2002

REGISTRATION NO.

24,156

(if appropriate)

Docket Number:

205,793

## **USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT**

This collection of information is required by 37 CFR 1.51. The information is used by the public to file (and by the PTO to process) a provisional application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 8 hours to complete, including gathering, preparing, and submitting the complete provisional application to the PTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, D.C., 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Box Provisional Application, Assistant Commissioner for Patents, Washington, D.C., 20231.

**PROVISIONAL APPLICATION COVER SHEET**  
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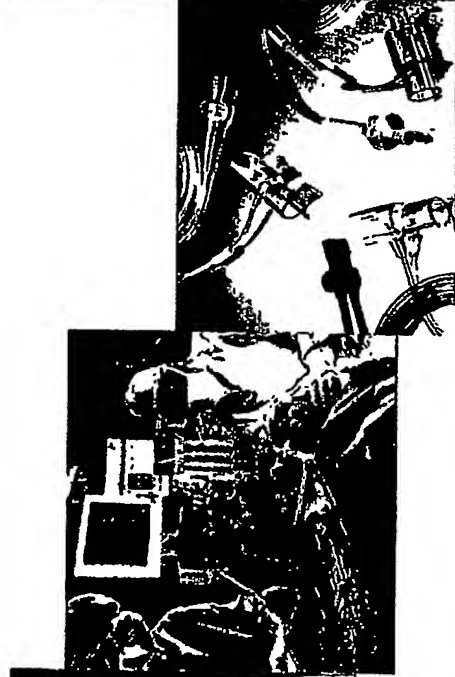
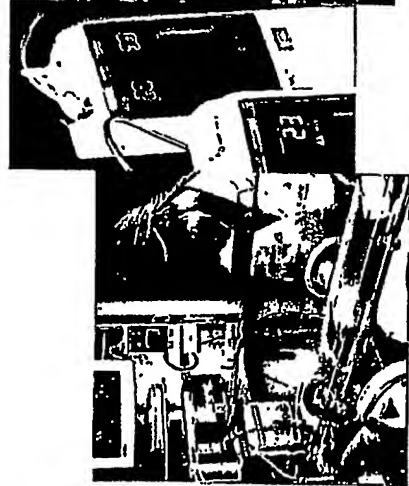
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Docket Number		205,793	Type a plus sign (+) inside this box →	+
INVENTOR(S) APPLICANT(S)				
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# Confidential and Proprietary Presentation

Enabling technologies  
for improved medical care



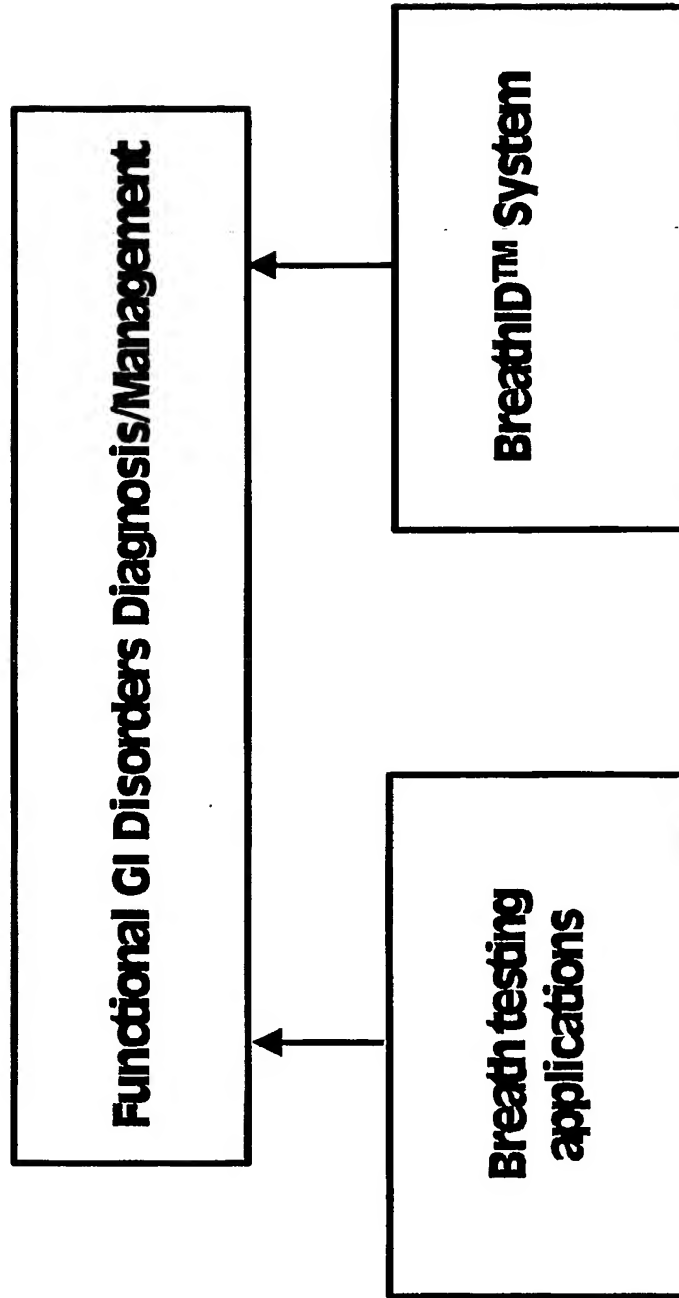
BreathID™ – State-Of-The-Art Tool for  
Breath Testing



Oridion

CONFIDENTIAL PRESENTATION

# Oridion BreathID's Target



# Why BreathID™ ?

- Reduction in drug development duration – effective & efficient research tool
- Enables therapeutic & diagnostic synergy - accurate, cost effective & convenient
- One stop device enabling the management of most GI disorders
- Cutting edge technologies – patent protected

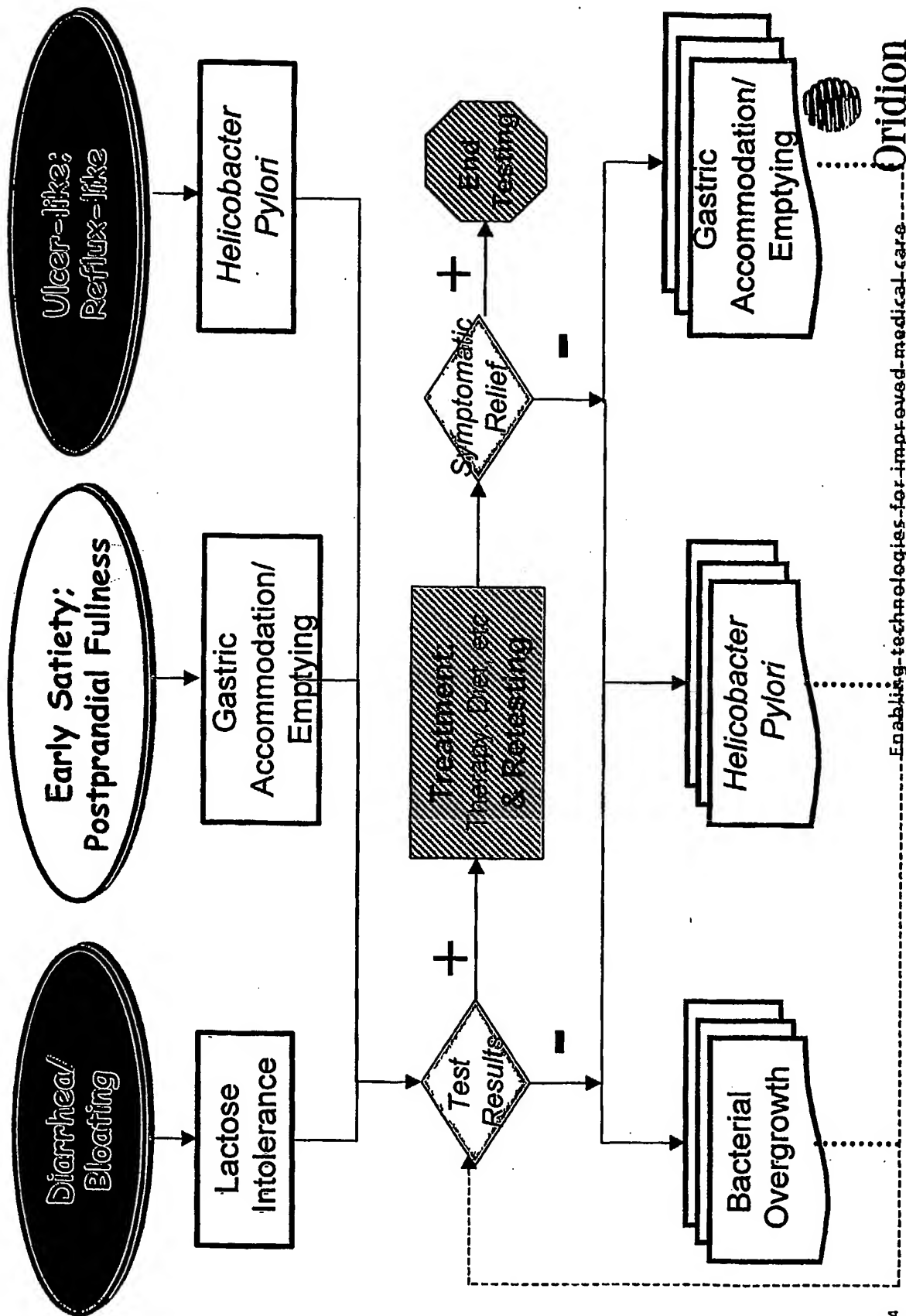


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# An Example for Management of Patients with Functional GI Disorders

Following the most intense symptoms



# Principles of Oridion's Gastric Accommodation Breath Tests (GABT)

The test is based on monitoring of gastric emptying using nutrient liquid meals.

Why does it make sense?

- 1) Accommodation of the stomach to a meal requires proximal stomach relaxation enabling volume increase without a rise in pressure.
- 2) The proximal stomach has a major role in liquid emptying and minor role in emptying of solids.
- 3) Inhibition of gastric emptying is required for meals with high nutrient content.
- 4) The distal stomach has a relatively minor role in emptying of liquids.

⇒ *Defective accommodation of the proximal stomach could be detected by accelerated emptying rate of an high volume nutrient liquid meal.*



# Background from scientific and clinical literature

## Surgical procedures:

- Resection of the fundus or vagal denervation of the proximal stomach in dogs increases intra-gastric pressure and accelerates emptying of liquids [1-3].
- Patients who have undergone vagotomy without “drainage” procedure exhibit accelerated emptying [4].

## Models based on clinical and scientific data:

- Recent models show that emptying of liquids is mandated by “Pressure Pump” and not “Peristaltic Pump” [5].

## Clinical Experience:

- Inhibition of gastric emptying to offset the increased delivery of calories to the duodenum is not always sufficient after a particular large meal [6].

## Pharmacological interventions:

- Cholecystokinin and gastrin inhibit proximal gastric contractions, decrease intragastric pressure and slow the emptying of liquids. Motilin produces reversed effects. Shown in humans and dogs [7-10].

## Studies on dyspeptic patients vs. controls

- It was shown that abnormal intra-gastric distribution in the liquid phase correlates with early satiety symptoms [11].

## Partial list of references

1. Strunz, U.T and Grossman M.I., *Am. J. Physiol.* 234: E552- E555, 1980.
2. Wilbur, B. G. and Kelly K. A., *Ann. Surg.* 178: 295-302, 1973.
3. Wilbur, B. G. et al, *Am. J. Physiol.* 226: 1445-1449, 1974.
4. Lavigne, M. E., et al, *Am. J. Surg* 138: 644-651, 1979.
5. Indreshkumar K., et al, *Am J. Physiol.* 278: G604-G616, 2000.
6. Moore, J.G., et al, *Dig. Dis. Sci.* 29: 513-519, 1984.
7. Hunt, J. N. and Ramsbottom, N., *Br. Med J.* 4: 386-387, 1967.
8. Dozois, R. R. and Kelly, K. A., *Am J. Physiol.* 221:113-117. 1971.
9. Debas, H. T., et al, *Gastroenterology* 68: 1211-1217, 1977.
10. Debas, H.T., et al. *Gastroenterology* 73: 777-780, 1977.
11. Piessevaux, H., et al, Submitted to publication (2002)



# Gastric Accommodation and Gastric Emptying Rate - simultaneously testing

- **Dual tests protocol:** gastric emptying rate is compared between two tests using a 200cc Ensure Plus meal and a 800cc Ensure Plus meal (the same Ensure but diluted with water)
- **Dual meals in single test protocol:** a second meal is administered during the emptying of the first meal. The same meals as in the dual tests protocol

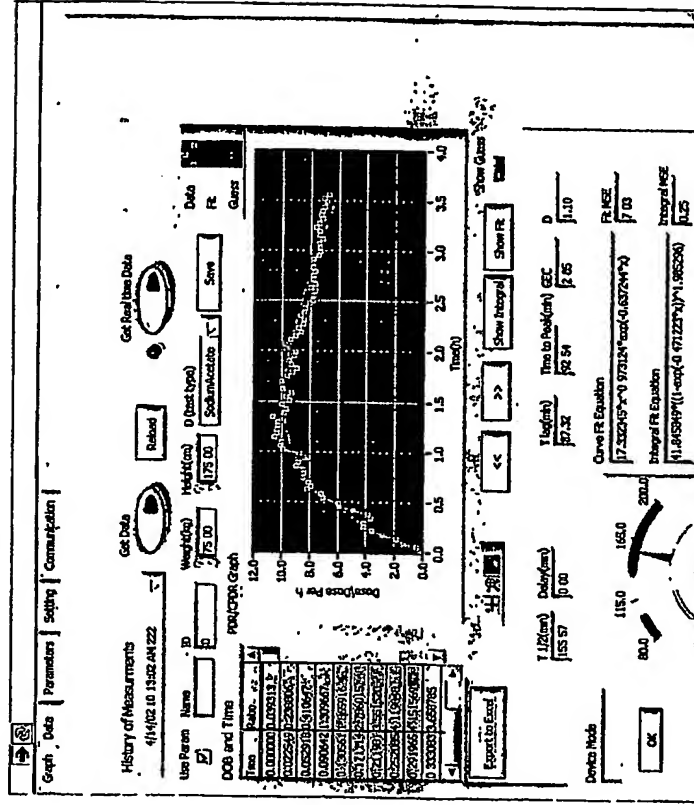
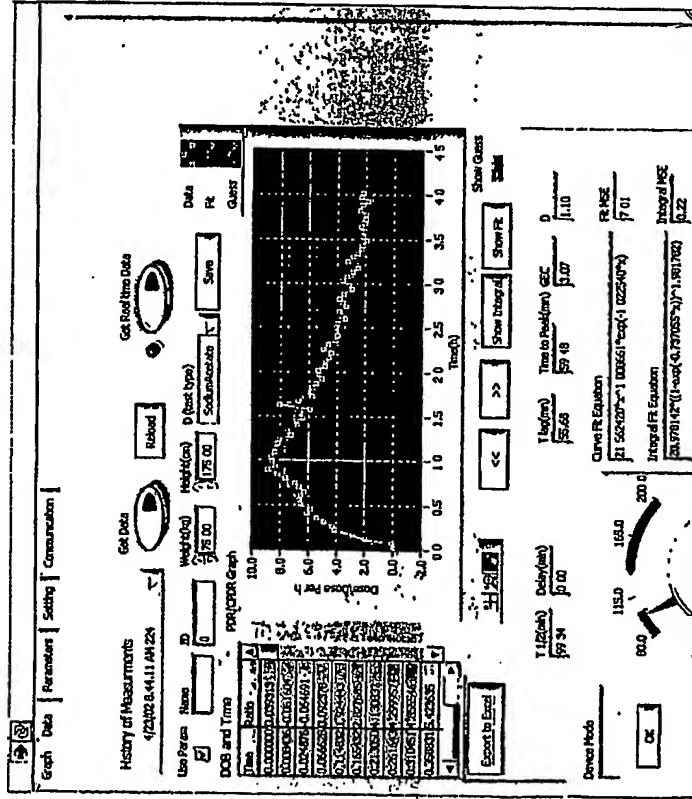


# Gastric Accommodation & Gastric Emptying Breath Testing (Dual Tests)

(Subject with early satiety)

800cc meal

200cc meal



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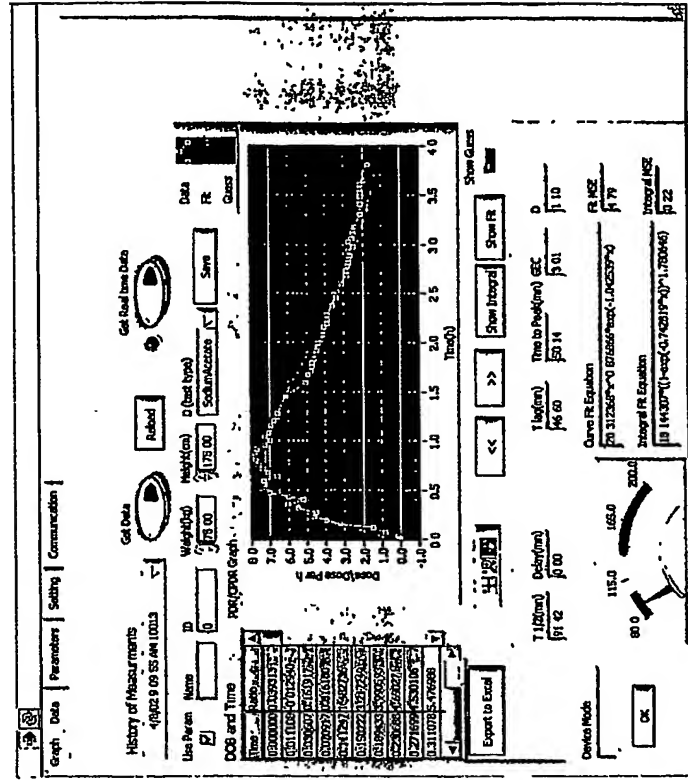
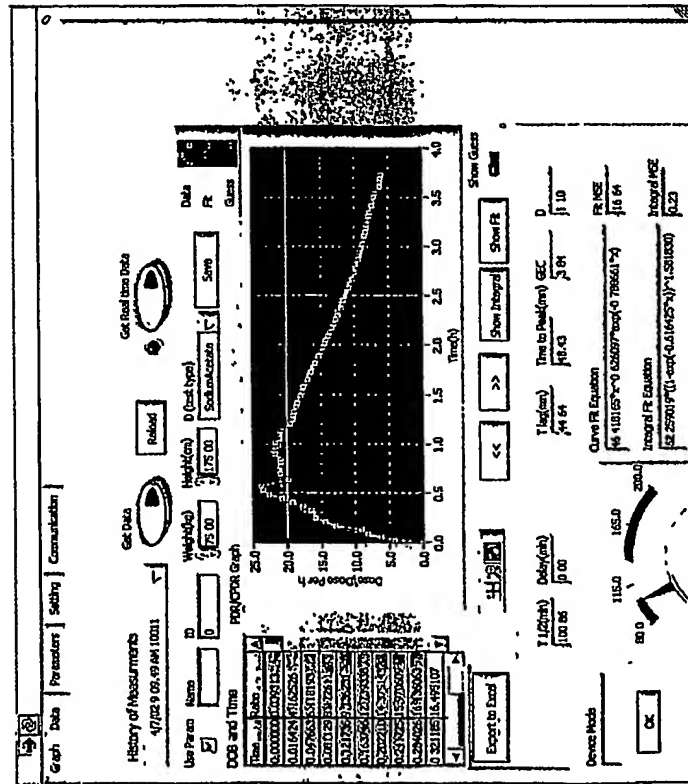
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# Gastric Accommodation & Gastric Emptying Breath Testing (Dual tests)

(Asymptomatic Subject)

800cc meal

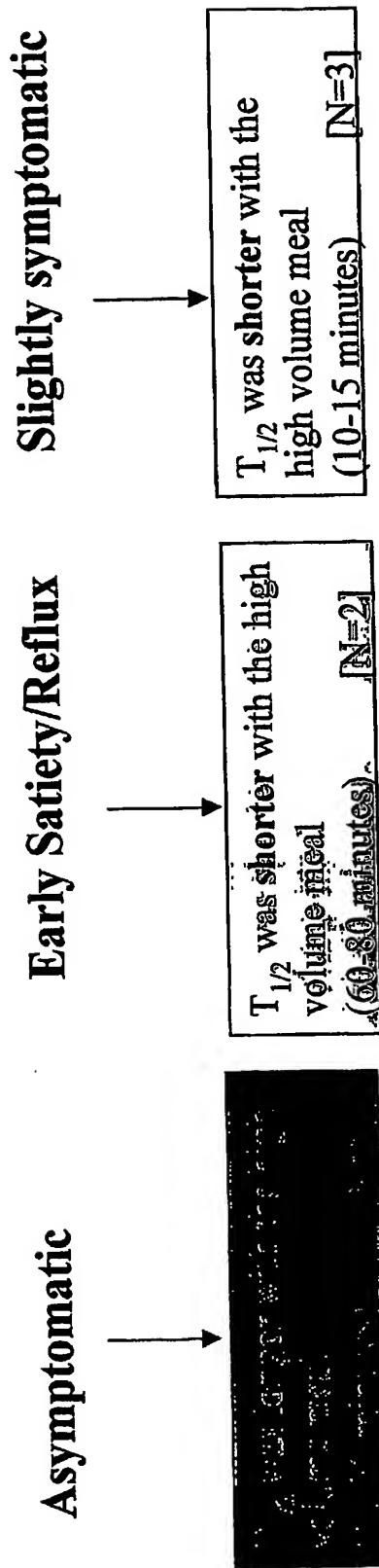
200cc meal



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# Results of the first ten subjects tested applying the dual tests protocol



These subjects were tested with two different drink volumes (200cc vs. 800cc) using the same nutrient content (300kcal).



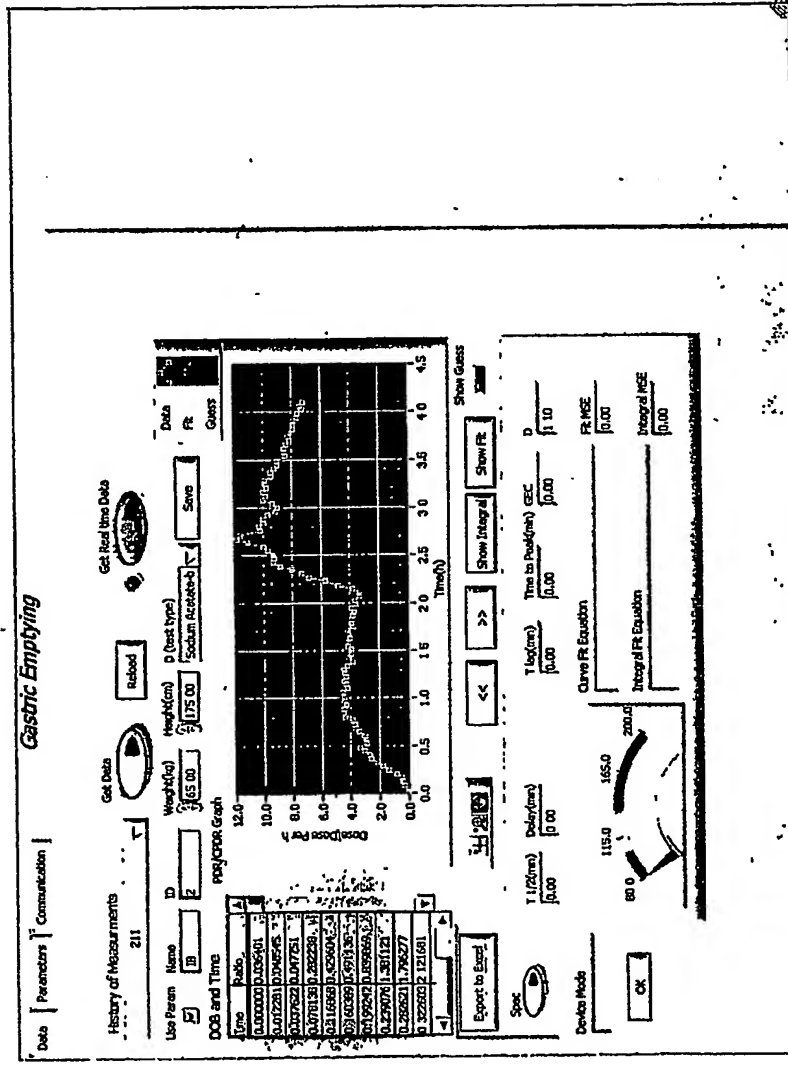
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# Gastric Accommodation & Gastric Emptying Breath Testing (Dual Meals)

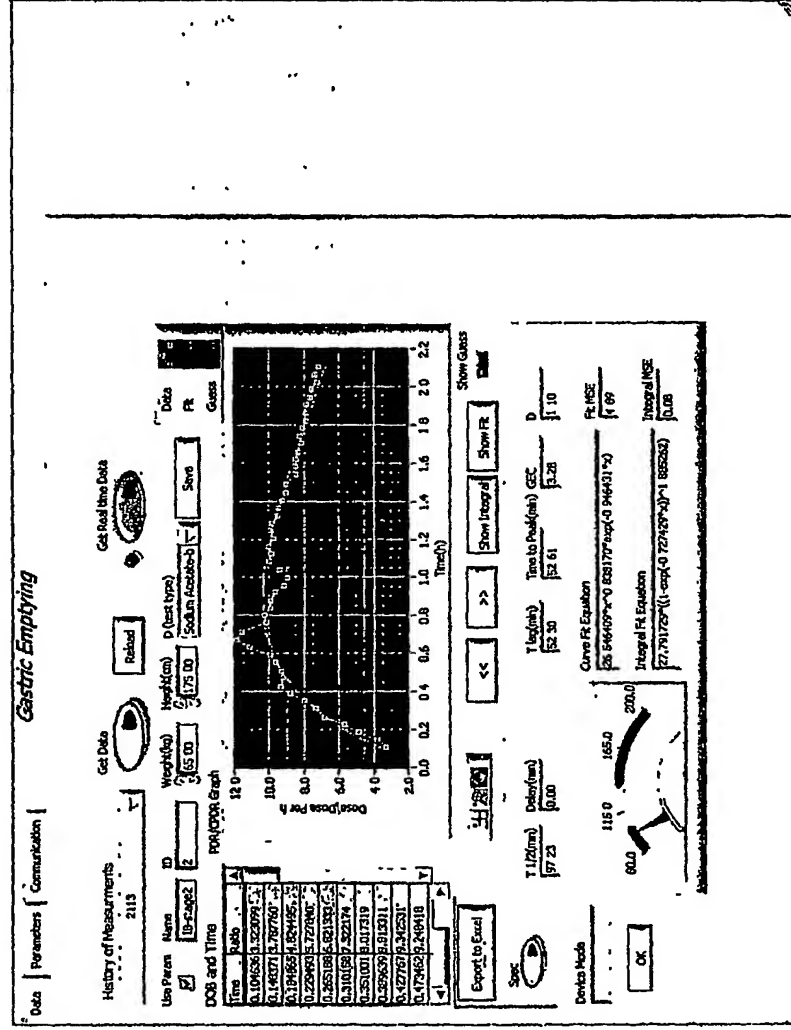
(Asymptomatic Subject)

A 200cc meal (with 50 mg  $^{13}\text{C}$  sodium acetate) is administered and one hour after the first peak a 800cc meal (with 100mg  $^{13}\text{C}$  sodium acetate) is administered.







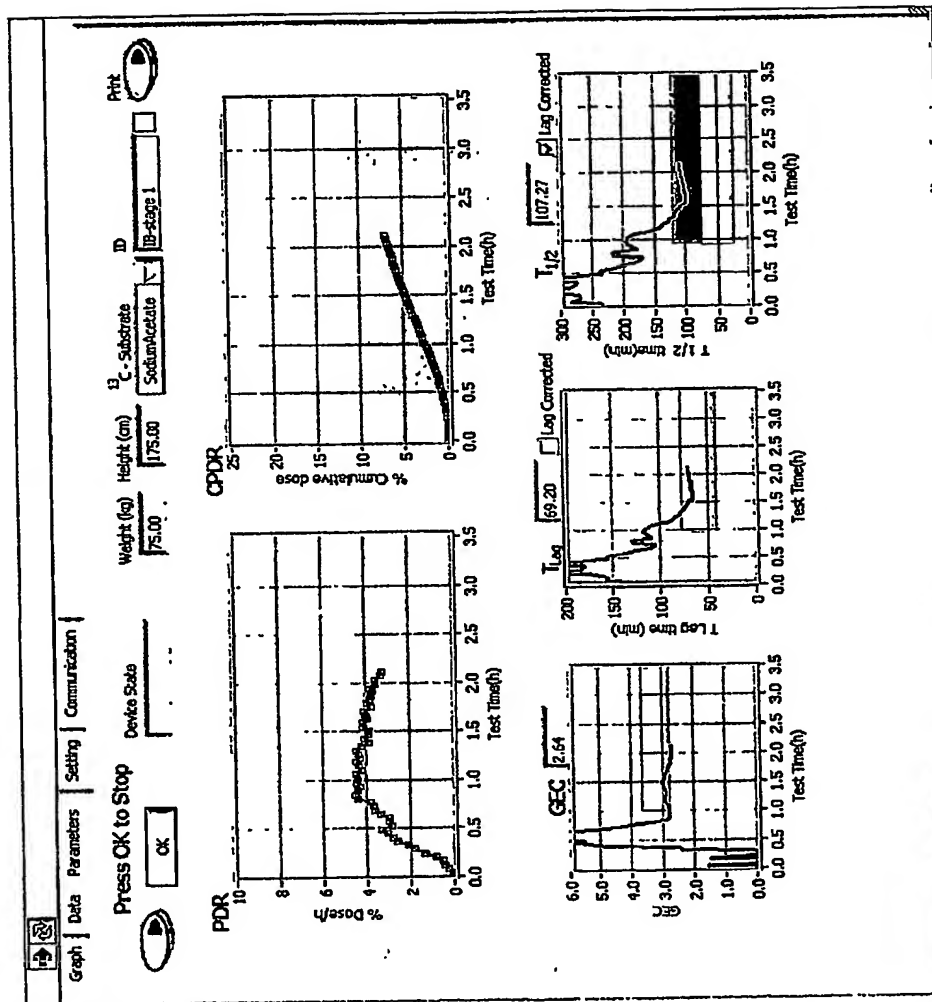


Graph 3.PDR of the second stage of the test meal -100 mg of <sup>13</sup>C sodium acetate as the marker. This was ingested after approximately 120 minutes from the beginning of the test.



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**Graph 4.** Several graphs describing the first stage of the test meal -50 mg of  $^{13}\text{C}$  sodium acetate as the marker. Clockwise beginning from the top left graph: PDR, CPDR (Cumulative Percentage Dose Rate- the integral of the PDR), mapping of  $T_{1/2}$ ,  $T_{\text{lag}}$  and Gastric Emptying Coefficient (GEC) as their derived values change and converge until the mathematical fit is complete.



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## Gastric Accommodation & Gastric Emptying Breath Testing (Dual Meals)

- If we record patient feedback to the two meals - in parallel to this procedure - we obtain in a single procedure:
  - Gastric Accommodation
  - Gastric Emptying Rate
  - Can distinguish if the patients has a sensation problem or a problem associated with the volume

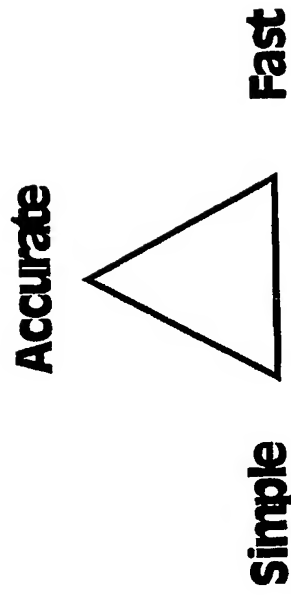


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# Real-Time Gastric Emptying Rate Breath Testing with the BreathID™

(using standard protocols and a solid meal)



**=>Field demand for the BreathID from people that are using laboratory breath tests or scintigraphy**

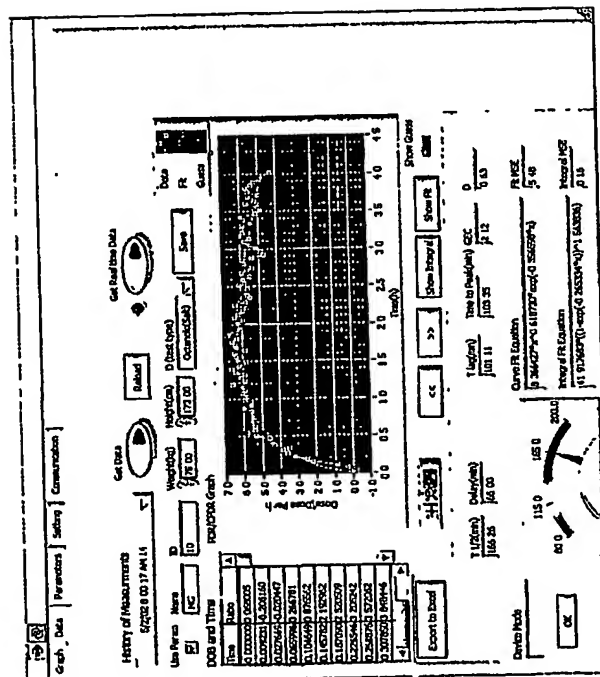
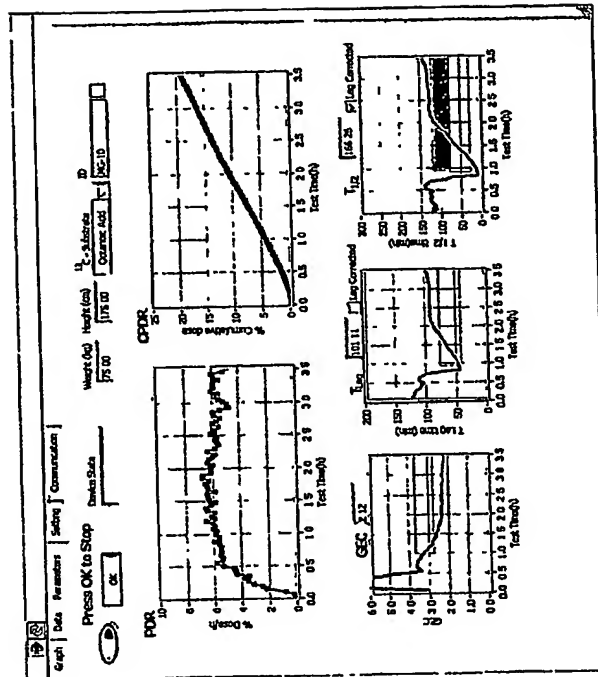


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# Example of a patient with Delayed Gastric Emptying (Diabetic Type 1)

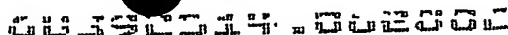


**Gastric Emptying Study Oridion / Hadassah-Spring 2002**  
**Subject 10-Type I Diabetic-Patient with Delayed Gastric Emptying Rate**



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**Gastric Emptying Study Oridion / Hadassah-Spring 2002**  
**Subject 1-Control Subject with Normal Gastric Emptying Rate**

# Continuous real time gastric emptying rate breath testing using the new BreathID™ System in diabetic patients and controls

Lysy Yosef<sup>1</sup>, Eran Goldin<sup>1</sup>, Michael Fried<sup>2</sup>

1- Hadassah University Hospital, Jerusalem, Israel

2- University Hospital Zurich, Zurich, Switzerland

**Introduction:** The objective of this study was to compare continuous real time breath testing using the BreathID™ System, to the standard method applying discrete sampling and mass spectrometry analysis for testing of gastric emptying rates.

**Results:** There was an excellent correlation between the BreathID™ and IRMS results ( $T_{lag}$ ,  $T_{1/2}$  and GEC with r values of 0.85, 0.88, 0.97 respectively,  $p < 0.0001$ ). The BreathID™ analyzes the results and provides  $T_{lag}$ ,  $T_{1/2}$  and GEC values throughout the test, resulting in a significant reduction of the test duration. Thus, results were obtained in all cases with normal gastric emptying rates within 2 hours.

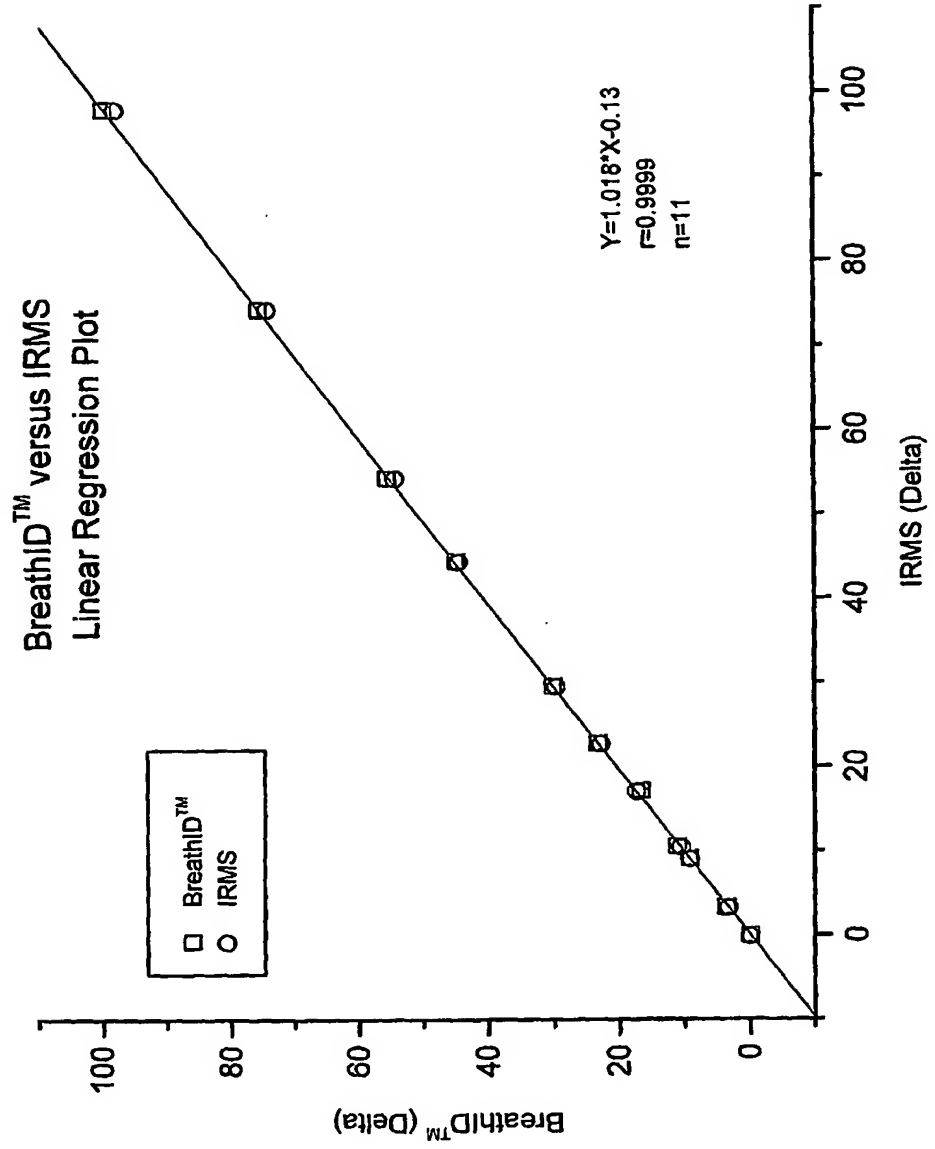
Full abstract could be found in the appendix



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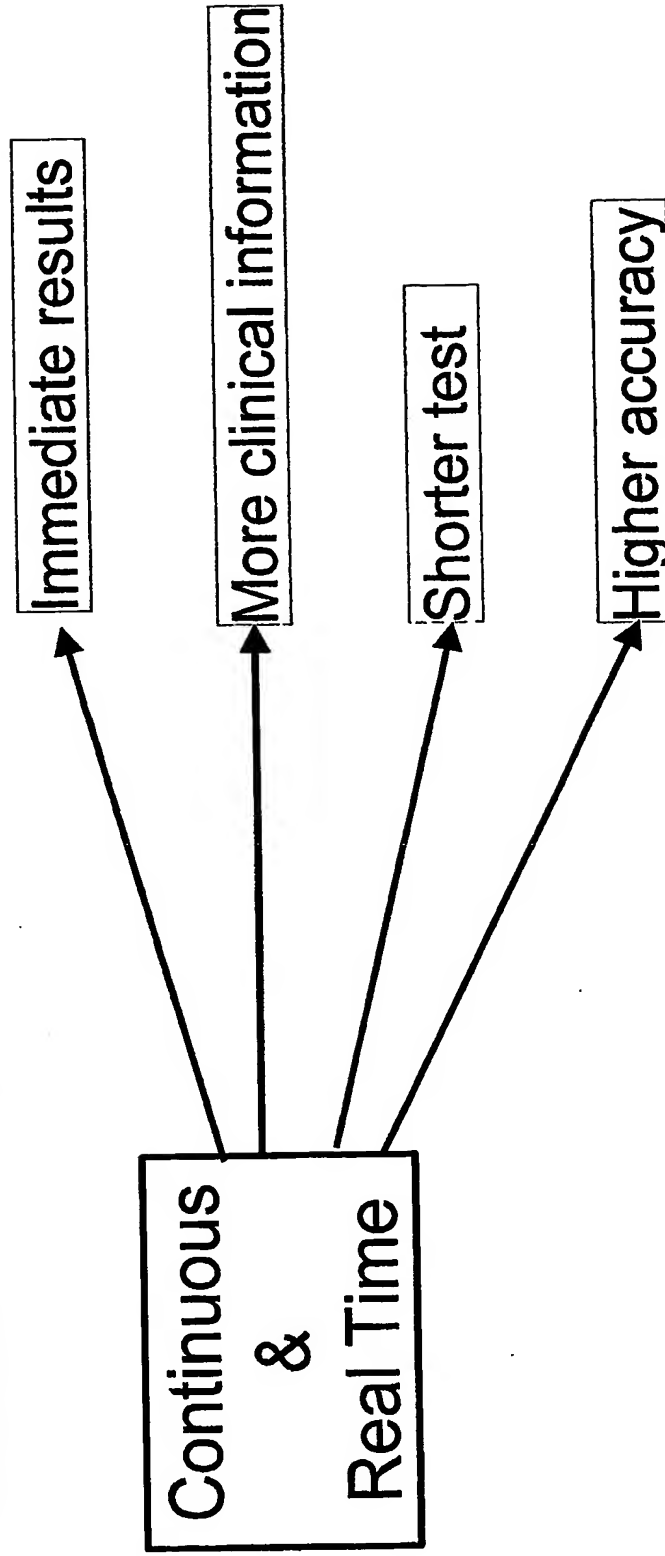
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# Direct Comparison BreathID™ vs. IRMS





# State of the Art Continuous Measurement



- Unparalleled accuracy of isotopic ratio reading
- Oridion's core technology – i.e. sensitivity & specificity higher than 99% in *H. pylori* diagnosis

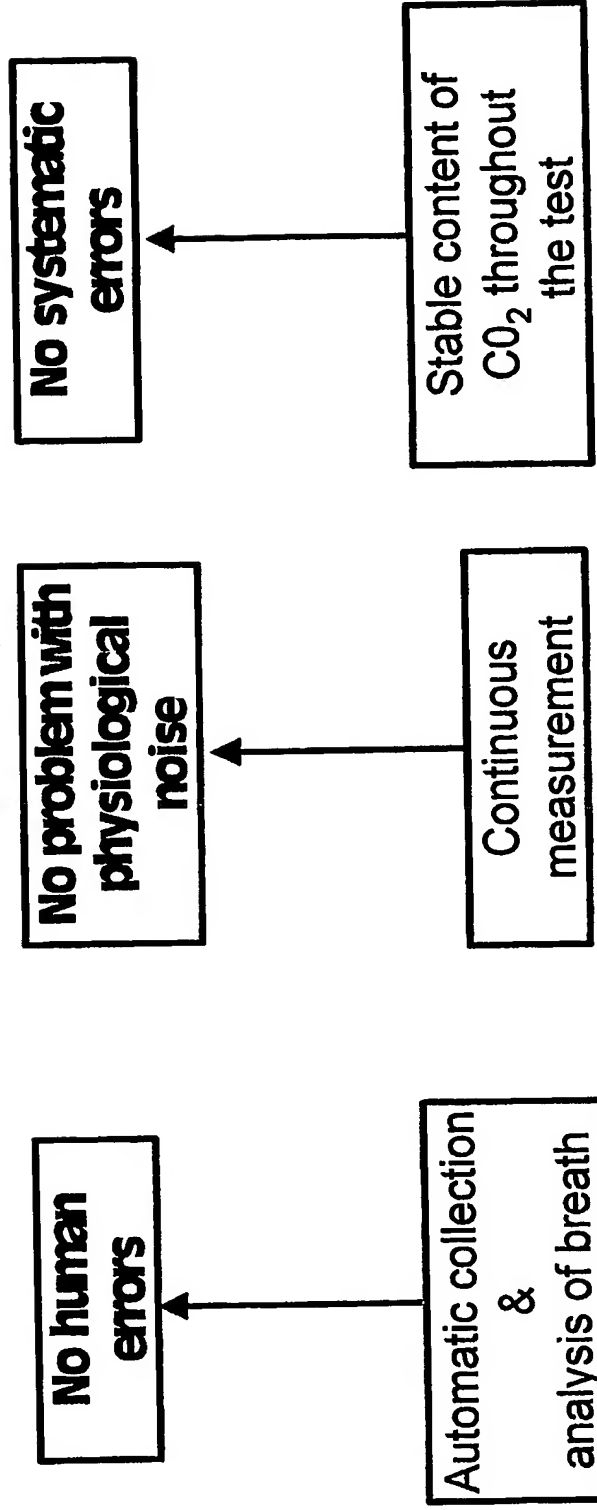
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# Accurate (cont)

## BreathID™ System assures



CO<sub>2</sub> FLOW - 0.5 L/min



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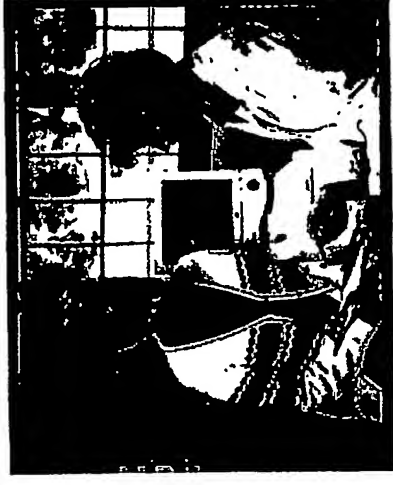
# Convenient & Flexible



- Single button operation
- Shorter tests due to real-time test analysis and ability to get results at early stages
- Management of GI disorders using one machine
- More appealing for patients
- Especially suitable for pediatric use



## Cost Effective



- Replaces expensive tests
- Minimal operator qualification and experience required
- Multi-application platform with the same device
- Minimizes number of consultations - immediate results
- Point of Care diagnosis



# BreathID™ - REAP the Benefits of Oridion's Unique Technology

- Research into new drugs made effective & efficient
- Enables synergy in routine clinical settings, between the therapeutic solutions and a diagnostic tool
- Allows multiple non-invasive POC diagnostic applications
- Patent protected technologies allowing extensive development



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# Appendix

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# Continuous real time gastric emptying rate breath testing using the new BreathID™ System in diabetic patients and controls

Lysy Yosef<sup>1</sup>, Eran Goldin<sup>1</sup>, Michael Fried<sup>2</sup>

1- Hadassah University Hospital, Jerusalem, Israel

2- University Hospital Zurich, Zurich, Switzerland

**Introduction:** The objective of this study was to compare continuous real time breath testing using the BreathID™ System, to the standard method applying discrete sampling and mass spectrometry analysis for testing of gastric emptying rates.

**Methods:** In this study, breath test analysis was performed on 15 diabetic patients (10 type 1 and 5 type 2) and 5 healthy control patients to monitor their gastric emptying rate. The subjects were investigated with the new BreathID™ System (Oridion BreathID), which automatically and continuously collects breath samples and displays results in real time. In parallel, breath samples were collected every 15 minutes for the first two hours and every 30 minutes for the rest of the test and sent to analysis by IRMS (Isotope Ratio Mass Spectrometer).

A standard meal using 100μl <sup>13</sup>C labeled octanoic acid dissolved in a scrambled egg with a pita bread was used (250 kcal). Analysis was performed according to a non-linear model [*Gastroenterology* 1993; 104:1640-7] to obtain T<sub>lag</sub>, T<sub>1/2</sub> and GEC. Breath samples were collected for 4 hours.

**Results:** There was an excellent correlation between the BreathID™ and IRMS results (T<sub>lag</sub>, T<sub>1/2</sub> and GEC with r values of 0.85, 0.88, 0.97 respectively, p<0.0001). The BreathID™ analyzes the results and provides T<sub>lag</sub>, T<sub>1/2</sub> and GEC values throughout the test, resulting in a significant reduction of the test duration. Thus, results were obtained in all cases with normal gastric emptying rates within 2 hours.

**Conclusions:** 1. The new BreathID™ test provides highly reliable data for on-line gastric emptying testing. 2. The BreathID™ allows convenient use and significant reduction of test duration, providing a tool to assess gastric emptying in clinical practice.

# Main Areas for BreathID™ Applications

- Helicobacter pylori – established test, in use in several countries
- Gastric motility
- Liver diseases
- Dyspepsia management
- IBS management
- Pancreas tests
- Satiety analysis
- Drug development and monitoring



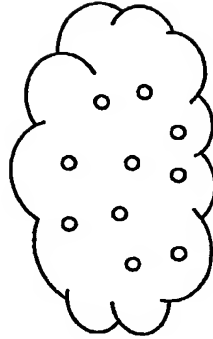
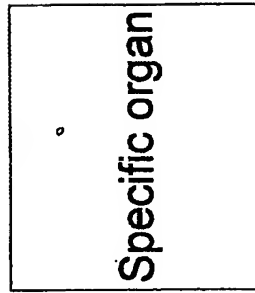
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# BreathID™ – Test Principles

" $^{13}\text{CO}_2$  Marked"  
exhalation

Test Meal + " $^{13}\text{C}$  Marker"



BreathID™  
"on the spot"  
test result



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# BreathID™ – Innovative Patient Management Tool

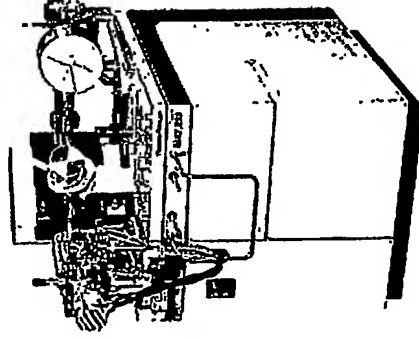
- Non-invasive tool for evaluation of internal organs & metabolic function
- BreathID™ enables breath tests to be performed and results obtained at the Point of Care - no need to send sample to the laboratory



# BreathID™ Advantages for Gastric Emptying Application Diagnosis

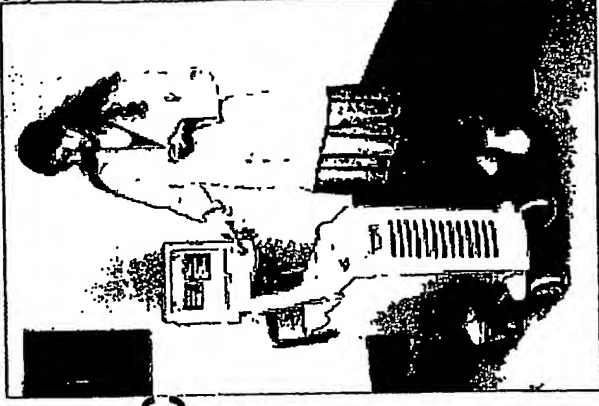
## Vs Lab Breath Tests

- More accurate
- Shorter tests
- Simple & convenient
- Immediate results



## Vs Scintigraphy

- Safer
- Cheaper
- Simple & convenient
- POC environment

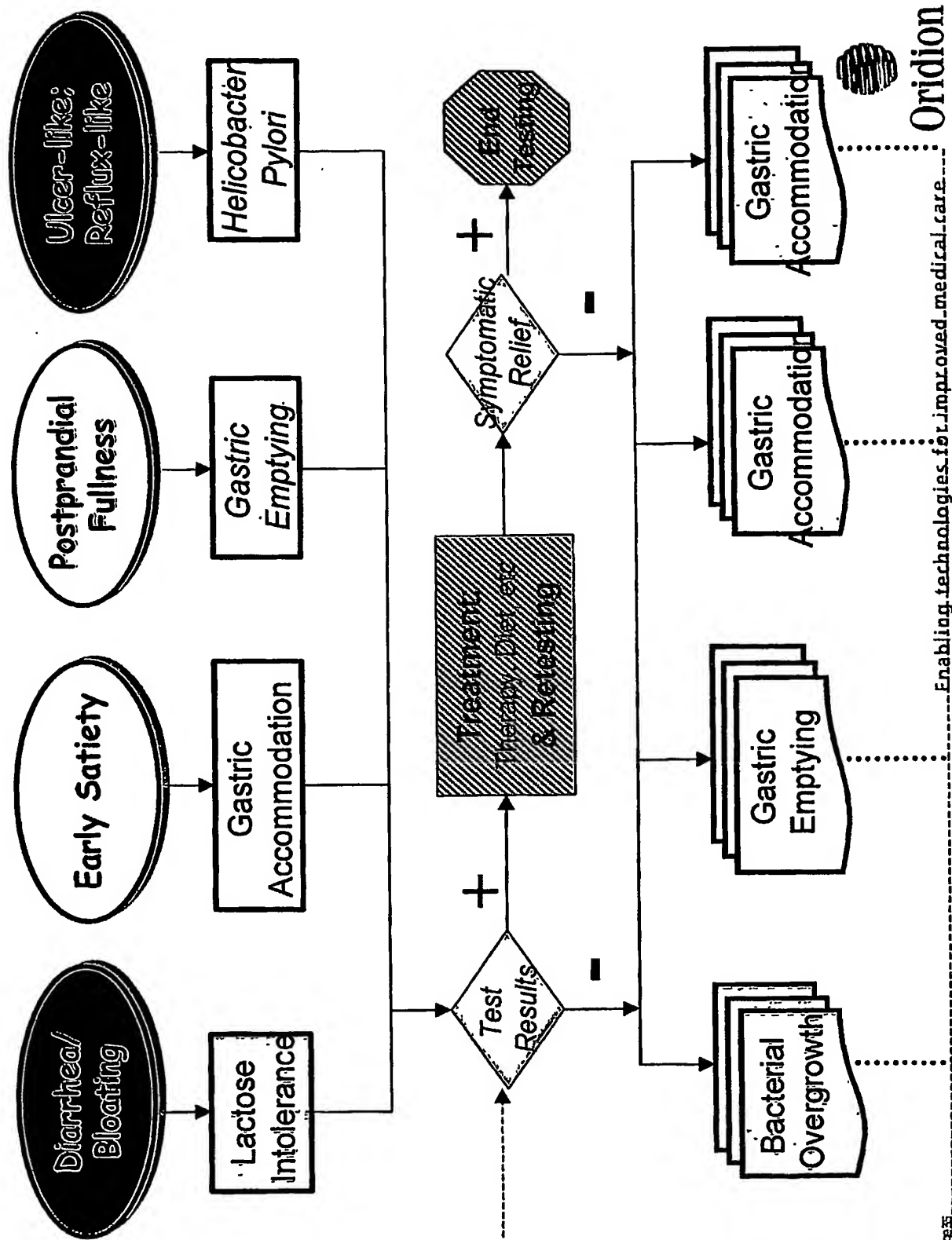


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# An Example for Management of Patients with Functional GI Disorders

Following the most intense symptoms



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